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(2) The homogeneity of the dose response lines for both the vaccine under test and the standard vaccine is acceptable;

(3) The log-dose response lines for the vaccine under test and the standard vaccine are shown to be parallel by an appropriate statistical method;

(4) The results of all dilutions shall be used to calculate the ED_{50} value of both the standard and test vaccine by a parallel line bioassay method or a method statistically equivalent;

(5) The challenge dose contains between 100 and 10,000 LD_{50} doses; and

(6) The LD_{50} value of the challenge suspension contains no more than 10,000 colony-forming units determined by plate count.

(f) *Repeat tests.* Repeat tests need be performed only on the serotype which failed to meet the potency requirements prescribed in paragraph (h) of this section. The results of each test on each serotype meeting the criteria in paragraph (e) of this section shall be combined by means of a geometric mean. The determination that the vaccine meets the potency requirements shall be made from the results of not more than three valid tests on each serotype.

(g) *Estimate of the potency.* The ED_{50} value of each vaccine shall be calculated. The protective unit value of each serotype per milliliter of the vaccine under test shall be calculated in terms of the unit value of the corresponding standard vaccine.

(h) *Potency requirements.* The vaccine shall have a potency of not less than 8 units per serotype per milliliter. This requirement shall be met only if the potency for a single test is not less than 4.4 units per serotype per milliliter, or for two tests not less than 5.3 units, or for three tests not less than 5.7 units.

[41 FR 18295, May 3, 1976, as amended at 41 FR 46587, Oct. 22, 1976]

§ 620.34 Mouse toxicity test.

The final vaccine shall be demonstrated to be free from toxicity by the following test: A group of no less than 10 and no more than 40 mice, each mouse weighing 14 to 16 grams, shall have free access to food and water at least 2 hours before injection and throughout the test period. The group weight of the mice shall be determined immediately before injection. Each mouse shall be injected intraperitoneally with a test dose of 0.5 milliliter of undiluted vaccine. The group weight of the mice shall be determined again at the end of 72 hours. The 72-hour average weight per mouse shall be no less than the average weight per mouse immediately preceding the injection. No more than 5 percent of the total number of mice used may die during the test period; however, neither death nor significant toxic signs attributable to the vaccine shall result.

[41 FR 18295, May 3, 1976]

§ 620.35 General requirements.

(a) *Freezing prohibition.* Cholera Vaccine shall not be frozen at any time.

(b) *Dose.* These standards are based on a total immunizing dose of two injections of 0.5 milliliter and 1.0 milliliter, respectively, given at intervals specified in the manufacturer's labeling.

(c) *Date of manufacture.* The date of manufacture shall be the date of initiation of the last valid potency test for the Ogawa serotype or the Inaba serotype, whichever date is earlier.

(d) *Labeling.* In addition to the applicable labeling provisions of this chapter, the package label shall bear the following: (1) A statement that the vaccine contains 8 units of each serotype antigen per milliliter.

(2) The statement, ''DO NOT FREEZE''.

(3) The statement, ''SHAKE WELL''.

(e) *Samples; protocols; official release.* For each lot of vaccine, the following material shall be submitted to the Director, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(1) A sample consisting of no less than 40 milliliters of the product. The sample may be in the final container or from the vaccine bulk lot.

(2) A protocol which consists of a summary of the history of manufacture of each lot including all results of each test for which test results are requested by the Director, Center for Biologics Evaluation and Research,